FILE

L15 ANSWER 25 OF 115 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1956:17370 CAPLUS
DN 50:17370
OREF 50:3641i,3642a-b
TI Photosensitization by chlorpromazine
AU Cohen, Irvin M.; Nash, Joe B.
SO Psychiat. Research Repts. (1955), No. 1, 11-13
DT Journal
LA Unavailable
AB Research was undertaken to ascertain whether or not **chlorpromazine** or its one known metabolite, the sulfoxide of **chlorpromazine**, induces photosensitization in humans on **topical** application, or if systemic absorption is required. Aqueous solns. containing 1% chlorpromazine and 1% chlorpromazine sulfoxide were applied to a small area of the skin, allowed to dry, and then exposed to sun lamp radiation. The erythema produced 5-6 hrs. after irradiation in the control area was at least equal to and more frequently was greater than that of the treated site in all patients.

L3 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:639545 CAPLUS
DN 117:239545
TI ChronoFilm: a novel transdermal and topical delivery system
AU Szycher, M.; Tabibi, E.; Siciliano, A.
CS PolyMedica Ind., Inc., Woburn, MA, 01801, USA
SO High Perform. Biomater. (1991), 807-12. Editor(s): Szycher, Michael. Publisher: Technomic, Lancaster, Pa.
CODEN: 58DCA6
DT Conference; General Review
LA English
AB A review with 4 refs. on controlled-release self-adhesive delivery systems for drugs based on biocompatible polyurethane elastomers (ChromoFilm) for transdermal and **topical administration**.

FILE

L6 ANSWER 21 OF 405 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:608526 CAPLUS
DN 129:184644
TI Method for reducing coronary artery reactivity using progesterone
IN Hermsmeyer, R. Kent
PA Dimera, LLC, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837897	A1	19980903	WO 1998-US3733	19980226
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6056972	A	20000502	US 1998-24972	19980206
	AU 9861866	A1	19980918	AU 1998-61866	19980226
PRAI	US 1997-806358	A	19970226		
	US 1998-24972	A	19980206		
	WO 1998-US3733	W	19980226		

AB A method for reducing coronary artery reactivity. A predetd. amount of natural progesterone is provided by a convenient and pleasant delivery system to the blood stream, sufficient to reduce the likelihood of coronary vasospasm and myocardial ischemia. The **progesterone** may be provided either by **topical** application to the epidermis of a cream in which the **progesterone** is dissolved or by patch technol., so as to provide continuous delivery and thereby maintain the level of **progesterone** in the blood stream at least about 1 ng per mL. Kits for dispensing the **topical progesterone** are also claimed. A method is also claimed for screening for compds. that can inhibit coronary vasospasm by testing them in exptl. animals, preferably rhesus monkeys, that have been treated with vasoconstrictive agents that invoke a coronary spasm; the vasoconstrictive agents are preferably serotonin and U46619.

FILE

L11 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:742241 CAPLUS
DN 129:347178
TI **Topical** antimicrobial compositions comprising **sphingosines** for use in cosmetics
IN Lambers, Johannes Wilhelmus Jacobus; Streekstra, Hugo
PA Gist-Brocades B.V., Neth.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9849999	A2	19981112	WO 1998-EP2795	19980504
	WO 9849999	A3	19990204		
	W: BR, JP, KR, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 914075	A2	19990512	EP 1998-928252	19980504
	R: DE, ES, FR, GB, IT				
	BR 9804872	A	19990824	BR 1998-4872	19980504
	JP 2000513745	T2	20001017	JP 1998-547751	19980504
	US 6147118	A	20001114	US 1998-214360	19981229
	KR 2000022503	A	20000425	KR 1998-710947	19981231
PRAI	EP 1997-201304	A	19970502		
	WO 1998-EP2795	W	19980504		

AB Topically occurring microbial growth is inhibited by applying a topical composition comprising a sphingoid base. Specifically, said sphingoid base is effectively formulated in combination with a surfactant. Antibacterial activity of sphingosine (I) against Staphylococcus aureus and Corynebacterium xerosis showed that the amount of colony forming units decreased with an increasing concentration of I from 0.005-0.02%. An anti-acne skin cleansing lotion contained PPG-26 buteth-26 and PEG-40 hydrogenated castor oil 1, phytosphyngosine 0.2, bu

FILE

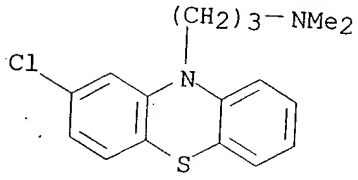
L3 ANSWER 20 OF 160 MEDLINE on STN
AN 1998010047 MEDLINE
DN 98010047 PubMed ID: 9349334
TI The effects of **topical doxepin** on responses to histamine, substance P and prostaglandin E2 in human skin.
AU Sabroe R A; Kennedy C T; Archer C B
CS University of Bristol, Department of Dermatology, Bristol Royal Infirmary, U.K.
SO BRITISH JOURNAL OF DERMATOLOGY, (1997 Sep) 137 (3) 386-90.
Journal code: 0004041. ISSN: 0007-0963.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971119
AB The tricyclic antidepressant, doxepin, is known to have H1 and H2 antihistaminic effects. Recently, 5% doxepin cream has been marketed in the U.S.A. for treatment of eczematous dermatoses. We investigated the effects of **topical doxepin** treatment on histamine-, substance P- and prostaglandin E2- (PGE2) induced responses in the skin of normal and atopic subjects. We compared the effects of **topical doxepin** with those of the oral antihistamine terfenadine. The weal volume and flare area responses to histamine were significantly reduced by treatment with **topical doxepin** or oral terfenadine in both normal and atopic subjects ($P < 0.05$). The mean +/- SEM percentage reduction in flare area for 10 micrograms/site of histamine in non-atopics and atopics was 48 +/- 8% and 60 +/- 17% with terfenadine, and 54 +/- 12% and 81 +/- 4% with **topical doxepin**, respectively. The mean percentage reduction in weal volume for the same dose of histamine in non-atopics and atopics was 70 +/- 9% and 63 +/- 16% with terfenadine, and 96 +/- 2% and 89 +/- 6% with **topical doxepin**, respectively. The flare but not the weal response to substance P was inhibited by both treatments in all subjects ($P < 0.05$). The mean +/- SEM percentage reduction in flare area for 200 pmol/site of substance P in non-atopics and atopics was 53 +/- 10% and 73 +/- 4% with terfenadine, and 74 +/- 7% and 75 +/- 4% with **topical doxepin**, respectively. The cutaneous responses to PGE2 were not affected by either drug. The inhibitory effects of doxepin were as great as those of terfenadine, and doxepin had a significantly greater effect than terfenadine in inhibiting the weal response to histamine and flare response to substance P in normal volunteers ($P < 0.05$). There was no significant difference between atopics and non-atopics in the percentage reduction of cutaneous responses by oral terfenadine or **topical doxepin**. Marked sedation occurred in three of the first 10 subjects treated with **topical doxepin**, necessitating a reduction in dosage for the remaining six subjects. In summary, **topical doxepin** was as effective as, and sometimes more effective than, a standard dose of oral terfenadine in the inhibition of histamine-induced and axon-reflex-mediated cutaneous responses. The marked sedative effect may limit its clinical use in some patients.

AUTHOR(S): Hepel, Maria; Mahdavi, Farah
CORPORATE SOURCE: Department of Chemistry, State University of New York at Potsdam, Potsdam, NY, 13676, USA
SOURCE: Microchemical Journal (1997), 56(1), 54-64
CODEN: MICJAN; ISSN: 0026-265X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new methodol. has been applied to drug release studies. A conductive polymer film was used as a matrix for drug incorporation. The characterization of the polymer films has been obtained by in situ monitoring of the mass change by a quartz crystal microbalance in conjunction with cyclic voltammetry. The electrochem. quartz crystal microbalance (EQCM) with its excellent sensitivity allowed direct measurement of the amt. of the drug released when the potential of the film was changed. New information on ion dynamics under the in situ conditions was obtained. The release of a neuroleptic drug, chlorpromazine (CPZ), from a composite polypyrrole/melanin film upon elec. stimulation has been studied.

IT **50-53-3**, Chlorpromazine, biological studies
RL: PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(application of the electrochem. quartz crystal microbalance for electrochem. controlled binding and release of chlorpromazine from conductive polymer matrix)

RN 50-53-3 CAPLUS
CN 10H-Phenothiazine-10-propanamine, 2-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)

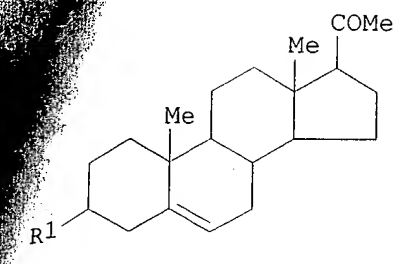


L234 ANSWER 11 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:144312 CAPLUS
DOCUMENT NUMBER: 126:190762
TITLE: **Melanin** formation inhibitors containing pregnenolones
INVENTOR(S): Hashizume, Ron; Ootsuki, Yoshikazu; Kamoda, Hironobu
PATENT ASSIGNEE(S): Adobansuto Sukin Risaachi Kenk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08337528	A2	19961224	JP 1995-148623	19950615

OTHER SOURCE(S): MARPAT 126:190762
GI

Searched by Barb O'Bryen, STIC 308-4291



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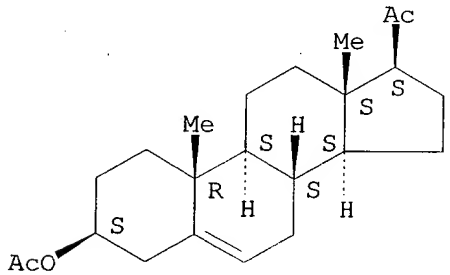
AB The **melanin** formation inhibitors contain pregnenolones I (R1 = C1-18 carboxyl, OH, OSO3H). Pregnenolone (at 25 .mu.M) showed significant whitening effect on cultured HM3KO cells (human skin **melanoma** cells). Formulation examples of ointments, skin lotions, and cosmetic packs are given.

IT **1778-02-5**, Pregnenolone acetate **33944-86-4**, Pregnenolone palmitate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pregnenolones as **melanin** formation inhibitors for **skin-lightening**)

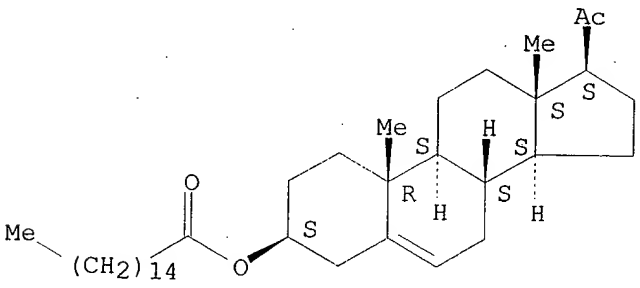
RN 1778-02-5 CAPLUS
CN Pregn-5-en-20-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 33944-86-4 CAPLUS
CN Pregn-5-en-20-one, 3-[(1-oxohexadecyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L234 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:143747 CAPLUS

Harris

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112

ACCESSION NUMBER: 93348096 MEDLINE
DOCUMENT NUMBER: 93348096 PubMed ID: 8346126
TITLE: Topical progesterone as treatment of choice in genital lichen sclerosis et atrophicus in children.
AUTHOR: Serrano G; Millan F; Fortea J M; Grau M; Aliaga A
SOURCE: PEDIATRIC DERMATOLOGY, (1993 Jun) 10 (2) 201.
Journal code: 8406799. ISSN: 0736-8046.
PUB. COUNTRY: United States
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19930924
Last Updated on STN: 19930924
Entered Medline: 19930909
CONTROLLED TERM: Check Tags: Female; Human; Male
Administration, Cutaneous
Child
Chronic Disease
*Genital Diseases, Female: DT, drug therapy
*Genital Diseases, Male: DT, drug therapy
*Lichenoid Eruptions: DT, drug therapy
***Pigmentation Disorders: DT, drug therapy**
*Progesterone: TU, therapeutic use
CAS REGISTRY NO.: **57-83-0 (Progesterone)**

L234 ANSWER 31 OF 45 MEDLINE
ACCESSION NUMBER: 89379530 MEDLINE
DOCUMENT NUMBER: 89379530 PubMed ID: 2777449
TITLE: The use of readily available photosensitizers for vitiligo in Nigeria.
AUTHOR: George A O
SOURCE: INTERNATIONAL JOURNAL OF DERMATOLOGY, (1989 Sep) 28 (7) 475-7.
Journal code: 0243704. ISSN: 0011-9059.
PUB. COUNTRY: United States
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891020
CONTROLLED TERM: Check Tags: Case Report; Female; Human
Adult
Child, Preschool
*Chlorpromazine: TU, therapeutic use
Nigeria
*Promethazine: TU, therapeutic use
Soaps
*Sunlight
***Vitiligo: DT, drug therapy**
CAS REGISTRY NO.: **50-53-3 (Chlorpromazine)**; 60-87-7 (Promethazine)
CHEMICAL NAME: 0 (Soaps)

L234 ANSWER 32 OF 45 MEDLINE
ACCESSION NUMBER: 88339384 MEDLINE
DOCUMENT NUMBER: 88339384 PubMed ID: 2844124
TITLE: Microprobe analysis of chlorpromazine pigmentation.
AUTHOR: Benning T L; McCormack K M; Ingram P; Kaplan D L; Shelburne J D
CORPORATE SOURCE: Department of Pathology, Duke University Medical Center, Durham, NC 27710.

Searched by Barb O'Bryen, STIC 308-4291

cleared after chlorpromazine was discontinued. They suggest that loxapine may be a suitable alternative to phenothiazines when skin pigmentation and ocular involvement occur, although the patient must be carefully monitored for ocular problems.

CONTROLLED TERM: Check Tags: Case Report; Human; Male
*Chlorpromazine: AE, adverse effects
Chlorpromazine: TU, therapeutic use
Chronic Disease
*Dibenzoxazepines: TU, therapeutic use
*Eye Color: DE, drug effects
*Loxapine: TU, therapeutic use
Middle Age
Photosensitivity Disorders: CI, chemically induced
*Schizophrenia: DT, drug therapy
***Skin Pigmentation: DE, drug effects**
CAS REGISTRY NO.: 1977-10-2 (Loxapine); **50-53-3 (Chlorpromazine)**
CHEMICAL NAME: 0 (Dibenzoxazepines)

L234 ANSWER 36 OF 45 MEDLINE
ACCESSION NUMBER: 67014260 MEDLINE
DOCUMENT NUMBER: 67014260 PubMed ID: 5917622
TITLE: Therapy of Phenothiazine-produced skin pigmentation: a preliminary report.
THOR: Gibbard B A; Lehmann H E
URCE: AMERICAN JOURNAL OF PSYCHIATRY, (1966 Sep) 123 (3) 351-2. Journal code: 0370512. ISSN: 0002-953X.
JB. COUNTRY: United States
OCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
ANGUAGE: English
ILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
NTRY MONTH: 196612
NTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19661226
CONTROLLED TERM: Check Tags: Female; Human
*Ascorbic Acid: TU, therapeutic use
*Chlorpromazine: AE, adverse effects
*Penicillamine: TU, therapeutic use
*Pigmentation Disorders: CI, chemically induced
***Pigmentation Disorders: DT, drug therapy**
Schizophrenia: DT, drug therapy
CAS REGISTRY NO.: **50-53-3 (Chlorpromazine)**; 50-81-7 (Ascorbic Acid); 52-67-5 (Penicillamine)

L234 ANSWER 37 OF 45 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-340107 [37] WPIDS
DOC. NO. NON-CPI: N2002-267371
DOC. NO. CPI: C2002-097809
TITLE: Human lung-originated G protein-coupled receptor protein TGR19 and encoded DNA, for developing drugs to treat diseases of central nervous system, and circulatory system, inflammatory diseases and cancer.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): ITO, T; MIWA, M; MIYAJIMA, N; SHINTANI, Y
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Tamoxifen has been reported to have numerous physiological effects that are independent of the estrogen receptor, including sensitization of resistant tumor cells to many chemotherapeutic agents. Drug-resistant cells sequester weak base chemotherapeutics in acidic organelles away from their sites of action in the cytosol and nucleus. This work reports that tamoxifen causes redistribution of weak base chemotherapeutics from acidic organelles to the nucleus in drug-resistant cells. Agents that disrupt organelle acidification (e.g., monensin, bafilomycin A1) cause a similar redistribution. Measurement of cellular pH in several cell lines reveals that tamoxifen inhibits acidification of **endosomes** and **lysosomes** without affecting cytoplasmic pH. Similar to monensin, tamoxifen decreased the rate of vesicular transport though the recycling and secretory pathways. Organellar acidification is required for many cellular functions, and its disruption could account for many of the side effects of tamoxifen.

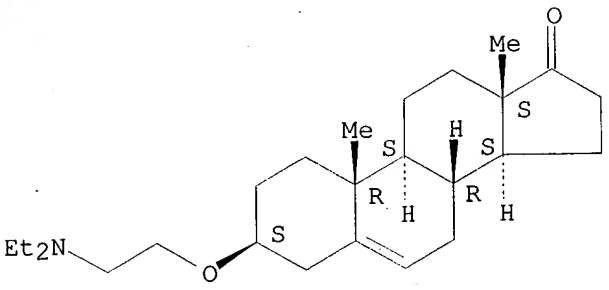
L84 ANSWER 22 OF 34 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998386460 EMBASE
TITLE: Effect of bafilomycin A1 and nocodazole on endocytic transport in HeLa cells: Implications for viral uncoating and infection.
AUTHOR: Bayer N.; Schober D.; Prchla E.; Murphy R.F.; Blaas D.; Fuchs R.
CORPORATE SOURCE: R. Fuchs, General/Experimental Pathology Dept., University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria. renate.fuchs@akh-wien.ac.at
SOURCE: Journal of Virology, (1998) 72/12 (9645-9655).
Refs: 74
ISSN: 0022-538X CODEN: JOVIAM

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Bafilomycin A1 (baf), a specific inhibitor of vacuolar proton ATPases, is commonly employed to demonstrate the requirement of low endosomal pH for viral uncoating. However, in certain cell types baf also affects the transport of endocytosed material from early to late endocytic compartments. To characterize the endocytic route in HeLa cells that are frequently used to study early events in viral infection, we used 35S-labeled human rhinovirus serotype 2 (HRV2) together with various fluid-phase markers. These virions are taken up via receptor-mediated endocytosis and undergo a conformational change to C-antigenic particles at a pH of <5.6, resulting in release of the genomic RNA and ultimately in infection (E. Prchla, E. Kuechler, D. Blaas, and R. Fuchs, J. Virol. 68:3713-3723, 1994). As revealed by fluorescence microscopy and subcellular fractionation of microsomes by free-flow electrophoresis (FFE), baf arrests the transport of all markers in early endosomes. In contrast, the microtubule-disrupting agent nocodazole was found to inhibit transport by accumulating marker in endosomal carrier vesicles (ECV), a compartment intermediate between early and late **endosomes**. Accordingly, **lysosomal** degradation of HRV2 was suppressed, whereas its conformational change and infectivity remained unaffected by this drug. Analysis of the subcellular distribution of HRV2 and fluid-phase markers in the presence of nocodazole by FFE revealed no difference from the control incubation in the absence of nocodazole. ECV and late endosomes thus have identical electrophoretic mobilities, and intraluminal pHs of <5.6 and allow uncoating of HRV2. As bafilomycin not only dissipates the low endosomal pH but also blocks transport from early to late endosomes in HeLa cells, its inhibitory effect on viral infection could in part also be attributed to trapping of virus in early endosomes which might lack components essential for uncoating. Consequently, inhibition of viral uncoating by bafilomycin cannot be taken to indicate a low pH requirement only.

Androst-5-en-17-one, 3-[2-(diethylamino)ethoxy]-, hydrochloride, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:150925 CAPLUS
DOCUMENT NUMBER: 130:295103
TITLE: Localization of Niemann-Pick C1 protein in astrocytes: implications for neuronal degeneration in Niemann-Pick type C disease
AUTHOR(S): Patel, Shutish C.; Suresh, Sundar; Kumar, Ujendra; Hu, C. Y.; Cooney, Adele; Blanchette-Mackie, E. Joan; Neufeld, Edward B.; Patel, Ramesh C.; Brady, Roscoe O.; Patel, Yogesh C.; Pentchev, Peter G.; Ong, Wei-Yi
CORPORATE SOURCE: Neurobiology Research Laboratory, Veterans Affairs Connecticut Healthcare System, Newington, CT, 06111, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(4), 1657-1662
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Niemann-Pick type C disease (NP-C) is an inherited neurovisceral lipid storage disorder characterized by progressive neurodegeneration. Most cases of NP-C result from inactivating mutations of NPC1, a recently identified member of a family of genes encoding membrane-bound proteins contg. putative sterol sensing domains. By using a specific antipeptide antibody to human NPC1, the authors have here investigated the cellular and subcellular localization and regulation of NPC1. By light and electron microscopic immunocytochem. of monkey brain, NPC1 was expressed predominantly in perisynaptic astrocytic glial processes. At a subcellular level, NPC1 localized to vesicles with the morphol. characteristics of **lysosomes** and to sites near the plasma membrane. Anal. of the temporal and spatial pattern of neurodegeneration in the NP-C mouse, a spontaneous mutant model of human NP-C, by amino-cupric-silver staining, showed that the terminal fields of axons and dendrites are the earliest sites of degeneration that occur well before the appearance of a neurol. phenotype. Western blots of cultured human fibroblasts and monkey brain homogenates revealed NPC1 as a 165-kDa protein. NPC1 levels in cultured fibroblasts were unchanged by incubation with low d. lipoproteins or oxysterols but were increased 2- to 3-fold by the drugs progesterone and U-18666A, which block cholesterol transport out

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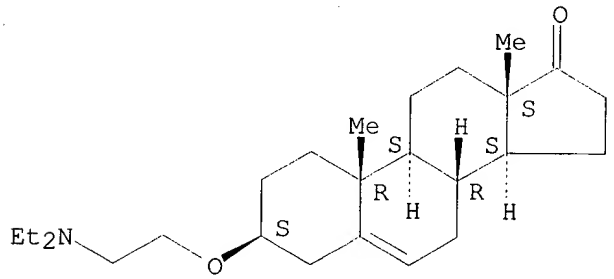
of **lysosomes**, and by the **lysosomotropic** agent NH4Cl. These studies show that NPC1 in brain is predominantly a glial protein present in astrocytic processes closely assocd. with nerve terminals, the earliest site of degeneration in NP-C. Given the vesicular localization of NPC1 and its proposed role in mediating retroendocytic trafficking of cholesterol and other **lysosomal** cargo, these results suggest that disruption of NPC1-mediated vesicular trafficking in astrocytes may be linked to neuronal degeneration in NP-C.

IT **3039-71-2**, U-18666A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Niemann-Pick C1 protein in fibroblasts of humans response to cholesterol transport-blockers progesterone and U-18666A and **lysosomotropic** NH4Cl)

RN 3039-71-2 CAPLUS

CN Androst-5-en-17-one, 3-[2-(diethylamino)ethoxy]-, hydrochloride, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:105930 CAPLUS
DOCUMENT NUMBER: 130:279626
TITLE: U18666A inhibits intracellular cholesterol transport and neurotransmitter release in human neuroblastoma cells
AUTHOR(S): Sparrow, Susan M.; Carter, Jodi M.; Ridgway, Neale D.; Cook, Harold W.; Byers, David M.
CORPORATE SOURCE: Atlantic Research Centre, Departments of Pediatrics and Biochemistry, Dalhousie University, Halifax, NS, B3H 4H7, Can.
SOURCE: Neurochemical Research (1999), 24(1), 69-77
CODEN: NEREDZ; ISSN: 0364-3190
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To det. if neurochem. function might be impaired in cell models with altered cholesterol balance, we studied the effects of U18666A (3-.beta.-[(2-diethyl-amino)ethoxy]androst-5-en-17-one) on intracellular cholesterol metab. in three human neuroblastoma cell lines (SK-N-SH, SK-N-MC, and SH-SY5Y). U18666A (.ltoreq.0.2 .mu.g/mL) completely inhibited low d. lipoprotein (LDL)-stimulated cholesterol esterification in SK-N-SH cells, while cholesterol esterification stimulated by